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BULK PROCESSING OF RADIONUCLIDE GENERATOR PARENTS AT THE LOS ALAMOS HOT CELL FACILITY

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Introduction

Bulk radionuclide processing at Los Alamos includes isotopes with short-lived radioactive daughter nuclides ("generator parents") for medical applications. The generator radionuclide parents ^{68}Ge, ^{82}Sr, ^{88}Zr and ^{109}Cd are regularly processed at the Los Alamos Hot Cell Facility. Nuclear chemical aspects related to the production and processing of these generator parents are briefly outlined below.

Radionuclide production and processing

Germanium-68 ($T_{1/2}$ = 270.8 d) solely decays via electron capture (EC) to ^{68}Ga, a positron emitter ($T_{1/2}$ = 67.6 min, β^+ 88%), which finds use in Positron Emission Tomography [1].

^{68}Ge can be obtained at lower proton energies via ^{69,71}Ga(p,xn) reactions using 36 MeV protons and gallium metal targets, which is the production route currently pursued within the U.S. DoE Medical Radioisotope Program. Irradiated Ga targets are mechanically removed from Nb capsules, and dissolved in aqua regia. The ^{68}Ge activity is then first extracted from the aqueous phase using tetrachloromethane. The overall processing yield is typically > 92 %, with respect to the theoretical thick target yield (1586 ± 30) MBq / μAh of the radionuclide.

Strontium-82 ($T_{1/2}$ = 25.5 d, EC=100%) is primarily used to generate the PET diagnostic radioisotope ^{82g}Rb ($T_{1/2}$ = 1.3 m), which has been utilized in myocardial perfusion studies [2]. At Los Alamos, ^{82}Sr is produced via the process ^{nat}Rb(p,xn)^{82}Sr using Rb metal or RbCl targets. In the case of Rb metal targets, the alkaline metal is dissolved in propanol, and the resulting rubidium alkylate, in turn, is decomposed with aqueous HCl. The obtained RbCl solution is evaporated to dryness. The product is further purified using anion exchange, and the $^{82}Sr^{2+}$ is retained on a chelation column, while Rb^+ elutes. Subsequently, $^{82}Sr^{2+}$ is desorbed from the column with HCl (6 molL^{-1}), and evaporated to dryness. Further purification is accomplished with an additional cation exchange step. The final product species is $^{82}SrCl_2$ (1-44 GBq per batch, 90-98% of the theoretical yield).

Cadmium-109 ($T_{1/2}$ = 462.6 d, EC=100%) has been suggested as a generator parent nuclide for ^{109m}Ag. Being a pure gamma emitter (IT=100%, Eγ=88.03 KeV) with a short half-life ($T_{1/2}$ = 39.6 s), ^{109m}Ag possesses properties of a single photon emission spectrometry (SPET) imaging radionuclide; the short half-life qualifies it especially for use with first pass radionuclide angiography [3]

The ^{109}Cd/^{109m}Ag generator has been under investigation at Los Alamos [4]; it is based on Cd/Ag separation via sorption on a column of particulate tin phosphate as an ion exchanger, which is loaded with ^{109}Cd contained in a slightly acidic matrix. ^{109m}Ag is eluted from the column using physiologically (phosphate) buffered solution accompanied by a reducing agent like dextrose or ascorbic acid and a complexing agent (thiosulfate). Thus, Ag^+ is

released from the column and reduced to Ag^0 and –as contained in a biologically inert matrix- immediately ready for injection. The breakthrough ratio of undesirable ^{109}Cd has been determined to be less than 10^{-7}.

^{109}Cd processed at Los Alamos is predominantly obtained from targets containing pure In metal of natural isotopic composition, irradiated with proton beams of 65 MeV incidental energy. Experimental $^{nat}In(p,x)^{109}Cd$ cross section values [5] were compared to ALICE-IPPE modeling results. It was found that the model is in good agreement for the low energy part of the excitation function, while values differ strongly for energies > 50 MeV. The corresponding thick target yield curve is shown in Figure 1.

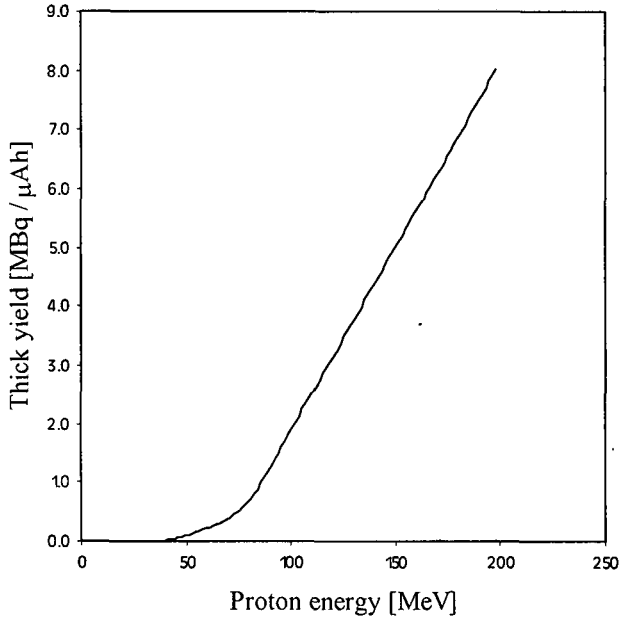

Fig. 1. Thick target yield function for the process $^{nat}In(p,xn)^{109}Cd$ calculated from the smoothed excitation function

Indium targets are dissolved in HCl, and contacted with an anion exchanger, where Cd is retained. The exchanger is washed with HCl, and Cd is subsequently eluted with HNO_3 and the solution is evaporated to dryness. The dry residue is again taken up in a small volume of HCl, and loaded onto a second anion exchange column, which is then treated with HCl of increasing concentration (gradient elution), whereby isotopes of In, Rh and Ag are removed. Cd is then eluted with concentrated HCl, while Sn isotopes remain on the solid phase. ^{109}Cd is assayed indirectly by detection of γ-rays of the daughter ^{109m}Ag after reaching quasi in-growth equilibrium. γ-ray counting results are compared against a liquid $^{109}Cd/^{109m}Ag$ standard source. Decontamination factors for In, Rh, Sn and non-^{109m}Ag silver isotopes are >500. Typically, 80 % of the theoretical ^{109}Cd activity can be recovered experimentally.

Zirconium-88 (83.4 d, EC=100%) is the parent nuclide of ^{88}Y (106.7 d, $\varepsilon+\beta^+$), which. has been considered a useful label surrogate for ^{90}Y in cancer radioimmunotherapy [6]. Although the half-life of the daughter is longer than the parent's, the system $^{88}Zr/Y$ practically appears as a generator. Within the distribution program at Los Alamos, ^{88}Zr is recovered from proton irradiated Nb capsules and beam windows irradiated with protons of 65 MeV incidental energy. To the best of our knowledge, experimental reaction cross section for the process

^{93}Nb(p, α2n+2p4n) ^{88}Zr have not been published as yet. Figure 2 shows the theoretical excitation function as predicted by ALICE-IPPE.

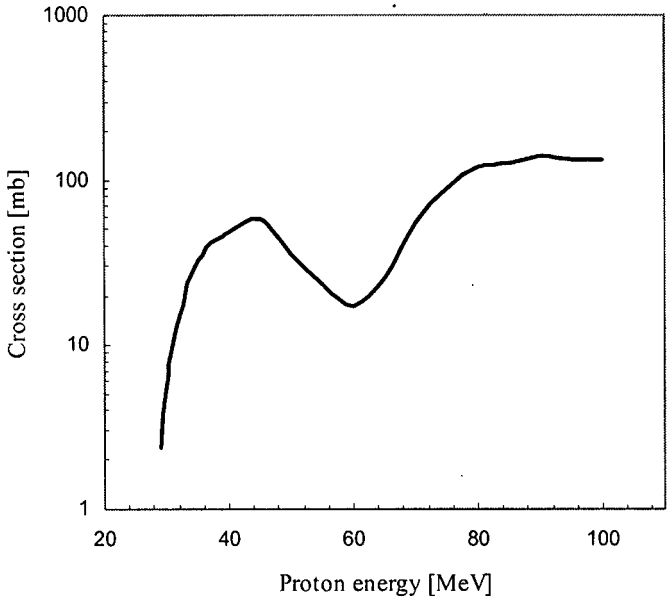

Fig. 4. ALICE-IPPE model calculation results for the process ^{93}Nb(p,α2n+2p4n) ^{88}Zr: accumulative reaction cross sections

Proton irradiated Nb target windows are carefully dissolved in HNO_3 /HF. In order to remove any traces of Y carrier, the solution is then contacted with a cation exchanger resin. The eluting Y mass depleted ^{88}Zr containing solution constitutes a liquid "reverse phase" radionuclide generator, and it is kept in stock.

After ^{88}Y activity in-growth, the isotope is separated by passing through a cation exchanger, where ^{88}Y is retained on the solid phase. The column is washed, and ^{88}Y with an extremely high specific activity is subsequently eluted with HNO_3. Yttrium-88 separation batches typically yield to 6 – 300 mCi of ^{88}Y, and overall experimental ^{88}Zr product yields amount to ~89 % of the theoretical thick target value [514.3 MBq(13.9 mCi)/μAh] calculated from ALICE-IPPE modeled cross section data.

Conclusion

The Los Alamos Hot Cell Facility regularly prepares bulk amounts of radionuclide generator isotopes mainly for medical applications. Targets irradiated at different sites are shipped to Los Alamos for chemical processing. Radiochemical separation methods based on liquid-liquid extraction and ion exchange were specifically developed or modified to suit remote control operations in a hot cell. Product radioisotope preparations meet the requirements of the Food and Drug Administration for pharmaceutical precursors.

Overall experimental yields generally correspond to more than 90% of the theoretical thick target yields calculated on the basis of reaction cross section data. Comparison of experimental reaction cross sections with ALICE-IPPE model calculation results confirm the notion that the underlying model describes nuclear processes on medium-mass target nuclei in a satisfactory manner, while giving poor results for heavier target elements.

Radionuclide shipments occur 1-6 times yearly with batch nuclide activities ranging from 40 MBq to 75 GBq.

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